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DOES BEETROOT JUICE LOWER BLOOD PRESSURE?: A SYSTEMATIC REVIEW**Maya Erisna^{*}, Merisa Restiani Arma, Sri Sumarni, Hilma Triana***Master of Applied Science in Midwifery, Poltekkes Kemenkes Semarang, Semarang, Indonesia*

Corresponding author's e-mail: mayaerisna@gmail.com

ABSTRACT

Background: Hypertension or high blood pressure has been a common global health problem for several years. The content of nitrate within beetroot helps to increase production of nitric oxide (NO) which serves as a vasodilator and has potency to reduce blood pressure. This study aims to determine the potential effect of beetroot juice on reducing blood pressure.

Methods: This study was a systematic review based on the PRISMA protocol as a writing guideline. Data were obtained from PubMed, Science Direct, and Google Scholar databases. Keywords used consisted of "beetroot", "beetroot juice", "blood pressure", and "hypertension." The eligibility criteria were research written in English, years of publication from 2014 and above, and Randomized controlled trials of beetroot juice interventions on reducing blood pressure.

Results: The literature search resulted in 376 records, and only 9 studies were in the systematic review. Six out of 9 studies showed significant results of blood pressure reduction, but the other three studies confirmed otherwise. A significant reduction of blood pressure was mostly observed in healthy subjects. The efficacy of beetroot juice supplementation is influenced by several factors, including gender, age, nutritional status (BMI), initial blood pressure, duration of supplementation, dose, and concentration of nitrate.

Conclusions: Beetroot juice supplementation is not so useful on reducing blood pressure because it only has an acute effect in lowering blood pressure and its effects were also influenced by several factors.

Key Words: beetroot juice, blood pressure, hypertension, a systematic review

INTRODUCTION

Hypertension has been a common global health problem for several years [1]. According to a study by Bloch in 2016, there were at least 1.39 billion people around the world suffering hypertension, around 31% of all adult population [2]. Complications caused by hypertension are estimated to have killed at least 9.4 million people each year worldwide, entailed by 45% of deaths from heart disease and 51% of deaths from stroke [3]. Currently, Hypertension is one of the non-communicable diseases that still becomes a problem in Indonesia. Data from the Basic Health Research (Riskesdas) in 2018 showed that around 34.1% of Indonesia's population had hypertension while in 2013 it was 25.8 %. It means that the prevalence of hypertension is rising [4].

Nutrition and lifestyle-based interventions are recognized as essential strategies for primary prevention and non-pharmacological alternative methods for treating hypertension [5]. Decreasing weight, exercising or increasing physical activity, quit smoking, and avoiding alcohol consumption are good lifestyle strategies to prevent hypertension [6]. Meanwhile, the recommended diet includes eating fruits and vegetables, reducing sodium consumption, or following the DASH (Dietary Approaches to Stop

Hypertension) diet recommended by the Academy of Nutrition and Dietetics and the American Heart Association (AHA) [7]. The DASH Diet highlights the importance of increasing the intake of fruits and vegetables and proven antihypertensive effect [8].

One of the great DASH diet plans for hypertension is high organic nitrate supplementation. Nitric Oxide (NO) is a molecule that can perform many functions in the human body, especially in the cardiovascular system. NO helps cardiovascular system as an antiplatelet, anti-proliferative and vasodilator function [9]. Nitrates in beetroot will increase production of nitric oxide (NO), a molecule involved in vasodilation of arteries and blood vessels and causes blood vessels to dilate. When blood vessels are dilated, it means more blood flow throughout the body which will reduce heavy work of the heart. The content of inorganic nitrate in beetroots is very high, which is around 110-3670 mg of nitrate per kilograms [8]. Beetroots also has many health-beneficial ingredients such as carotenoids, flavonoids, vitamins, potassium, sodium, phosphorus, calcium, magnesium, copper, iron, zinc, manganese, sodium, and betalain (betacyanin).[10, 11].

Briefly, after consuming beetroot juice, inorganic nitrates are involved in complex cycles. Nitrates that have been digested are absorbed quickly in the stomach and small intestine so that they reach peak of plasma level which is around 30-60 minutes after consumption. Salivary gland takes 25% of the nitrate actively, secreted into saliva in oral cavity. Anaerobic bacteria on tongue reduce nitrate (NO_3^-) to nitrite (NO_2^-). This Saliva containing nitrite components is swallowed and reabsorbed in digestive system and into circulatory system. Then, some of these nitrite components are reduced to nitric oxide (NO) in stomach with an acidic environment and lack of oxygen (hypoxia). Some other components of nitrite will be absorbed into circulation. The remaining amount of nitrite will be reduced to NO in blood vessels through mechanisms with assistance of enzymes and non-enzymes including deoxyhemoglobin, deoxymyoglobin in skeleton and vascular, heart muscle, xanthine oxidase in endothelial cells, aldehyde oxidase, aldehyde dehydrogenase, cytochrome P-450, mitochondrial nitrite reductase (such as the mitochondrial electron transport complex) in all cells and polyphenols. After that, NO increases concentration of cyclic 3',5'-guanosine monophosphate in vascular smooth muscle cells. The resulting rise in cyclic 3',5'-guanosine monophosphate initiates Ca^{2+} extrusion from the smooth muscle cell, subsequently promotes vasodilatation and decreases blood pressure[12–17]. A Summary of the process is illustrated in Figure 1.

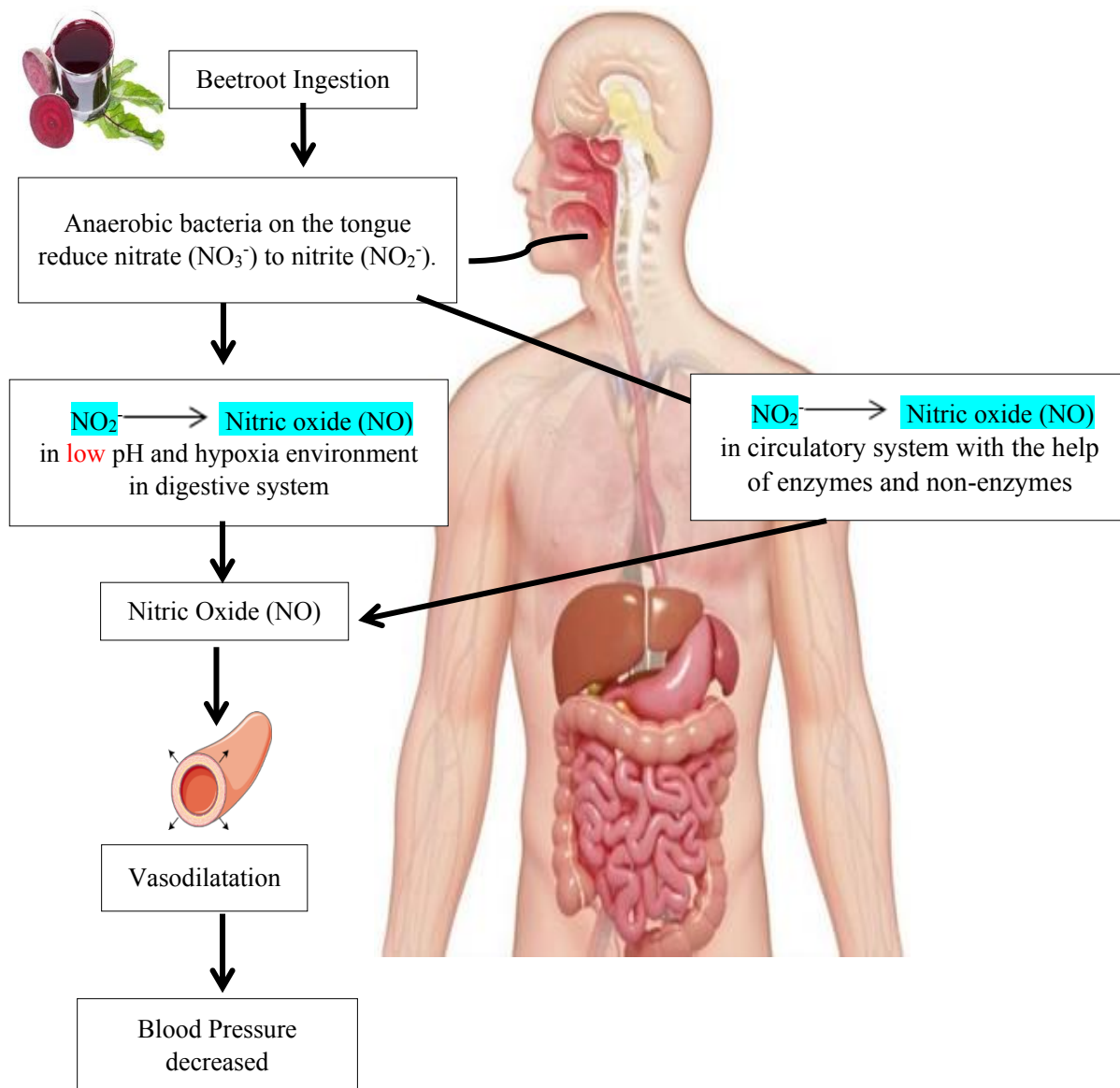


Figure 1 Summary of the antihypertensive effect of beetroot juice

Many studies have explored potency of beetroots, such as being able to improve exercise performance [18], endothelial function, and systemic anti-inflammatory [19]. The results of the study showed the increase in plasma nitrate and nitrite after 3 and 6 hours of consumption of beetroot juice. The average systolic and diastolic blood pressure relative decreased after 3 hours of consumption [20]. Short-term consumption of beetroot juice is recommended as a preventive measure, while long-term supplementation is recommended for treatment [21].

Nowadays beetroot is widely used as one of the ingredients in salad or weaning food. Beetroot also is known to be effective in increasing hemoglobin levels in anemic pregnant women [22] but is not widely used as an alternative to lower the blood pressure. In addition, studies investigating the antihypertensive effects of beetroot juice have showed different results. Therefore, the purpose of this study is to perform an up-to-date review of the effect of beetroot juice supplementation on blood pressure. We hypothesize that beetroot juice supplementation will reduce blood pressure as alternative prevention and treatment of hypertension.



METHODS

This study used systematic review based on the PRISMA (Preferred Reporting Items For Systematic Reviews & Meta-Analyses) Protocol as a writing guideline [23].

Searching Strategy and Data Sources

Literature search in this study was conducted through a Pubmed database search, Science Direct, and Google Scholar. The keywords used include "beetroot," "beetroot juice," "blood pressure," "hypertension." and also enriched with terms NOT exercise NOT sport. The literature selection after using the keywords resulted 2,397 publications from January 2014 to January 2019.

Eligible Criteria

The inclusive criteria in this study were: research written in English; year of publication starting from 2014 onwards, as this would cover the most recent of studies; Randomized Controlled Trial (RCT); Research providing intervention in beetroot juice; and research reporting the consumption of beetroot juice on blood pressure. The exclusive criteria in this study were (1) an editorial, review, and studies that did not correspond to original research, (2) studies with no control group; (3) studies that did not address the effects on blood pressure; (4) studies that discussed stamina, sports, and exercise; studies that discussed the types of hypertension due to other diseases (e.g., diabetes)

Data Extraction

Research article search was conducted from January 2019 to February 2019. Authors independently conducted article selection and data extraction. After the search of the published articles, the screening options of the databases were used to meet the inclusive criteria. Selected references were screened from the title, abstract, or full-text publication to identify studies that include relevance to serve as a reference. We also looked at the contents of the articles to easily categorize the factors affecting effectiveness of beetroot juice in decreasing blood pressure. The data were obtained and analyzed from the selected articles.

RESULTS

The literature selection after searching through keywords and "NOT" boolean operator resulted in 376 articles. There are 332 potentially eligible articles in total after duplication checking was carried out. The articles were screened by the time of publication, type of article, and availability of text, resulted in 134 articles. Articles that were not relevant to beetroot juice, hypertension, and blood pressure were discarded, leaving 68 articles. However, after checking the full text of each of the articles there were 47 articles focused on exercise and performance, 7 articles included another compound as supplements, 5 articles discussing other diseases and two others were not showing blood pressure result. Finally, 9 articles met the inclusive criteria. The literature search scheme is shown in figure 2.

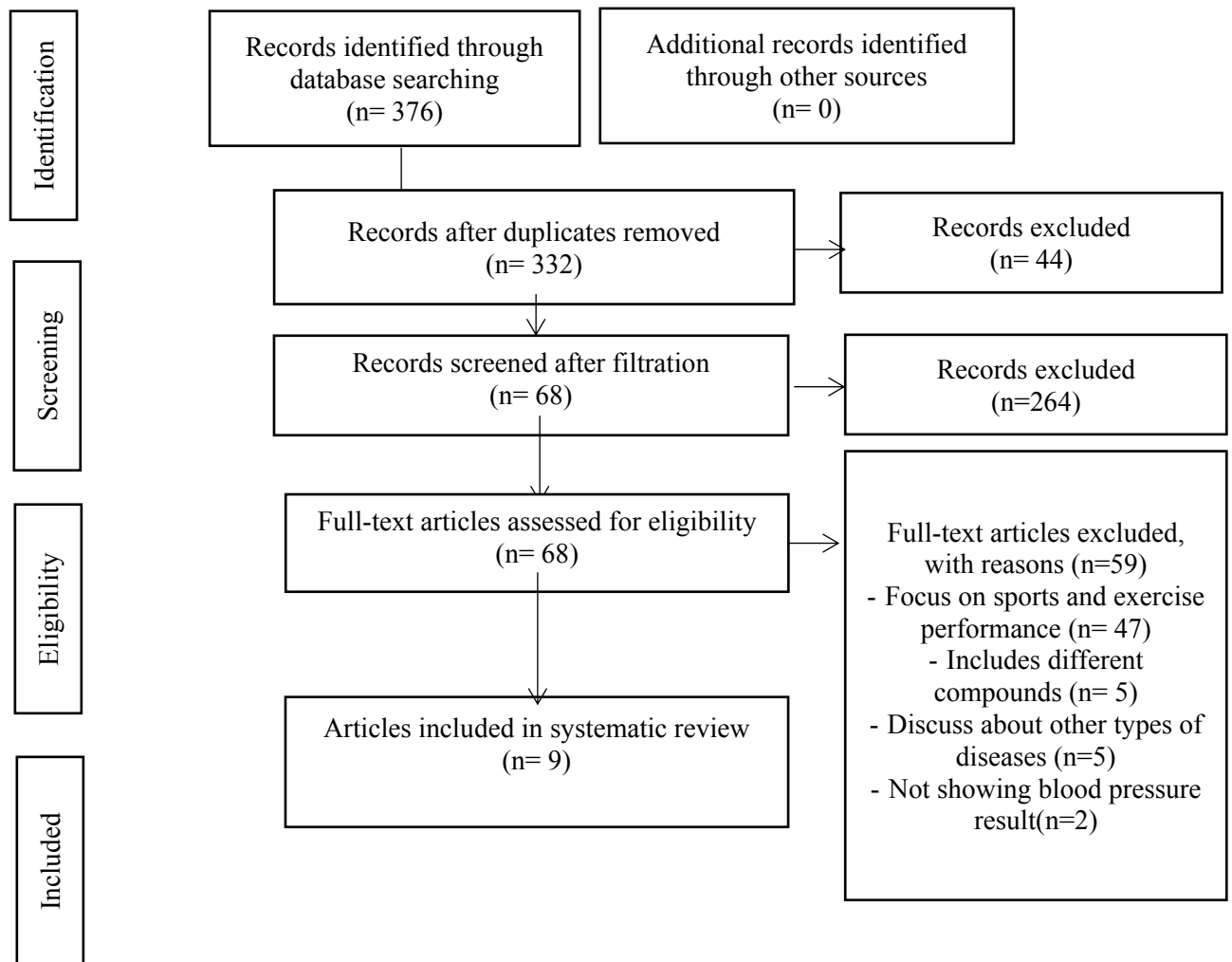


Figure 2 Systematic reviews (PRISMA) flow chart

The variety of participant characteristics and supplementation protocol would likely contribute substantial heterogeneity to the outcomes. Therefore, analyses were performed based on gender, age, BMI (Body Mass Index), and baseline blood pressure. We also categorized supplementation protocol by supplementation duration, dosage, and NO₃⁻ concentration. Finally, we performed a subgroup analysis based on placebo and beetroot juice purposes. Characteristic of each article are detailed in Table 1.

Table 1 Evidence for the effects of beetroot juice on blood pressure

Reference	Sample Population and Gender (M/F)	Age (Years) ; (Mean \pm SD)	BMI (kg / m ²); (Mean \pm SD)	Baseline Blood Pressure (SBP; DBP)	Supplementation Duration	BRJ Dosage (mL)	Placebo	NO ₃ ⁻ Concentration	Effect on SBP	Effect on DBP
M. Siervo, 2015 [5]	85 both (50 M; 35 F)	55–76 ;	20,2 – 39.5 (30.5 \pm 4.4)	(135.1 \pm 14.8; 77.4 \pm 9.5) (146.9 \pm 19.8; 79.3 \pm 8.5) (142.8 \pm 13.9; 81.1 \pm 9, .1) (131.6 \pm 16.0; 80.0 \pm 16.0; 80.0 \pm 9.57) mmHg	3 weeks; 1 week; 2 weeks	70 - 250	Yes (NO ₃ ⁻ depleted beetroot juice)	(\pm 4.5 mmol); (\pm 9.0 mmol); (\pm 7.5 mmol; (\pm 0.002 mmol) 300-400 mg	No statistically significant changes	No statistically significant changes
Bondonno., 2015 [24]	27, both (10 M; 17 F)	50 - 70 (63.2 \pm 4.4 y)	18 - 35 (26.9 \pm 3.2)	(132.9 \pm 11.8); (76.2 \pm 10.4) mmHg	1 week	140	Yes (NO ₃ ⁻ depleted beetroot juice)	8.06 mmol; 500 mg	No statistically significant changes	No statistically significant changes
Jajja, 2014 [25]	(12M; 9F)	55 – 70 (62.7 \pm 1.5)	25 – 40 (30.1 \pm 1.2)	(135.1 \pm 4.7; 77.1 \pm 15.4)	21 days	70	Yes (blackcurrant juice)	4.8-6.4 mmol; 300-400 mg	\downarrow 7.3 \pm 5.9 mmHg during the final week	No statistically significant changes

Kapil, [26]	2015	32 both (16M;16 F)	18 - 85	(26.5 ± 4.0)	(138.4 ± 17.1); (82.8 ± 11.2)	4 weeks	250	Yes (NO ₃ ⁻ depleted beetroot juice)	25.7 ± 5 · 3 mmol / L; 6.4 mmol	(Clinic SBP 7.7 mmHg) (ABP 7.7); (after 6 weeks ↓ 8.1 mmHg)	(DBP Clinic 2.4 mmHg); (ABP 5.2); (after 6 weeks ↓ 3.8 mmHg)
Raubenheimer, 2017 [20]		12 both (5M; 7F)	57 - 71	(25.7 ± 4.2)	133.0 ± 16.6; 88.6 ± 8.8	2 weeks	140	Yes (NO ₃ ⁻ depleted beetroot juice)	12.9 mmol	↓ 7.9 mmHg	↓ 5.7 mmHg
McDonagh, 2018 [27]		10 M	(24 ± 5)	none	115 ± 10 mmHg; 66 ± 6 mmHg	24 hour	55	Yes (NO ₃ ⁻ depleted beetroot juice, beetroot flapjack)	± 5.76 mmol	↓ 5 mmHg	↓ 3-4 mmHg
Asgary, [19]	2016	24 both (12M;12 F)	25 – 68	(24.91 ± 9.24)	132.50 ± 10.34 mmHg; 81.67 ± 8.35 mmHg	2 weeks	250	No	4.2 mmol - 8.4 mmol	↓ 6.67 mmHg	↓ 4.59 mmHg
Ormesher, 2018 [28]		40 F	>16 years	19.29 – 49.61 (29.97 ± 11.20)	130 mmHg; 80 mmHg	8 days	70	Yes (NO ₃ ⁻ depleted beetroot juice)	400 mg (92.4 ± 11.9 mmol)	No statistically significant changes	No statistically significant changes
Ashor, [29]	2015	21 both (12M; 9F)	55 – 70 (62.0 ± 4.5)	20 – 40 (29.9 ± 4.2)	135.1 ± 14.9; 77.5 ± 9.6	21 days	70	Yes (Blackcurrant juice)	300–400 mg	↓ 10 mmHg after 3 weeks	↓ 3 mmHg after 3 weeks of

M: Male; F: Female; BMI: Body mass image; BRJ: Beetroot juice; SBP: Systolic blood pressure; DBP: Diastolic blood pressure

Four studies were double blinded [5, 24, 26, 28], three studies were open-label [20, 25, 29] trials and two others were single blinded trial [19, 27]. The total number of participants included in this review was 272, with 10–85 participants per study. The inclusive criteria of studies in this review showed some variation. Siervo [5] recruited participants with age older than 55 years; Bondonno [24] recruited hypertensive participants who were taking between 1 and 3 antihypertensive medications; Jajja [25] and Raubenheimer [20] recruited nonsmoking older adult; Kapil [26] recruited participants with age between 18 and 85 years old, estimated glomerular filtration rate >50 mL/min, and blood pressure more than 130/85 mmHg; McDonagh [27] recruited healthy normotensive participants. Hypertensive adult that were not taking any antihypertensive medication were include in the study by Asgary [19]. Ormesher [27] recruited Pregnant women with chronic hypertension who were not taking anti-hypertensive medication, and who were between 22 and 35-36 weeks of gestation. Siervo [5], Bandono [24], and McDonagh [6] added some agreements such as avoiding mouthwash usage, limiting alcohol and caffeinated drink during the study period. Exclusive criteria between studies have some similarities. All studies excluded participants with any evidence of acute or chronic disease such as cardiovascular disease, pulmonary, musculoskeletal disease, osteoporotic fractures, cancer, and diabetes. Participants that smoking and taking any hypertensive medications, drugs, antibiotic, hormonal therapy also excluded in the studies [19, 25, 27, 28]. Study by Asgary [19] and Bondonno [24] pregnant women were excluded. Meanwhile, Ormesher [28] excluded pregnant women with multiple pregnancy.

Participant characteristic

Most participants were reported as female (n=145) and male (n=127). One study included only females [28] and one study included only males [27] and seven studies had both gender [5, 19, 20, 24–26, 29]. Four studies were conducted in older aged ranging from 50 – 85 years [5, 20, 25, 29], three studies recruited young adult participants [24, 27, 28] and two studies mixed the age of participants from young adult to older adult [19, 26]. The mean BMI of the participants ranged between 24.9 and 30.5 kg/m². Siervo [5], Jajja [25], and Ashor [29] recruited overweight or obese participants. The mean \pm SD baseline systolic blood pressure of participants ranged from 131.6 \pm 16.0 to 146.9 \pm 19.8. There are three [19, 24, 28] that recruited pre-hypertension or hypertensive participants and six others recruited healthy participants with normal blood pressure [5, 20, 25–27, 29].

Supplementation Protocol

Supplementation durations from 9 studies ranged from 24 hour to 21 days. The daily doses of beetroot juice consumed varied from 55 mL to 250 mL. McDonagh [27] used 55 mL of beetroot juice in his study. Jajja [25], Ormesher [28], and Ashor [29] gave 70 mL of beetroot juice to the subjects. Bondonno [24] and Raubenheimer [20] used 140 mL. Kapil [26] and Asgary [19] used 250 mL of beetroot juice, while Siervo [5] used 70 mL, 140 mL and 250 mL beetroot juice for three different group. The Concentration of NO₃⁻ varied between 300- 500 mg \approx 3 - 12.9 mmol beetroot juice. The volume of beetroot juice reported in the studies of this review ranged from 55mL to 250mL. The choice of the placebo varied between studies and included blackcurrant juice (2 studies) [25, 29] and nitrate-depleted beetroot juice (6 studies) [5, 20, 24, 26 – 28].

DISCUSSION

The Studies about beetroot juice supplementation showed mixed results. Most of them have clinical significance in decreasing blood pressure, but others showed otherwise. This result indicates that the efficacy of beetroot juice supplementation is influenced by several factors, such as respondent characteristics (gender, age, and body mass index) and supplementation of beetroot juice (duration, nitrate concentration, and volume).

Some studies have chosen more male sex than female [5, 25, 27, 29]. The beetroot juice supplementation had a more significant blood pressure-lowering effects on male respondents as compared to female because premenopausal female tended to have lower initial blood pressure limits

than that of male [30]. A Study by Cole and Clifton [31] showed that the trend of beetroot juice lowering blood pressure was stronger in males than in females to the point that when analyzing the groups separately after 6 hours post ingestion, SBP in males was decreased 4–5 mmHg and females 2–3 mmHg. In other hand, Siervo showed a different result that there was no significant difference in ambulatory blood pressure between male and female respondents [5]. Baiao [32] also stated that there was no difference between male and female levels of nitrate and nitrite after consumption of beetroot juice. These differences in results prove the importance of further research on the effect of beetroot juice supplementation based on gender.

One of the critical factors that affect the effectiveness of beetroot juice supplementation is age. Young adult subjects showed more effective results as compared to older adult subjects. Plasma nitrite levels after supplementation of beetroot juice are affected by changes in an age where changes in the microbiota in the mouth occur and enterosalivary area depletion [20]. There is some evidence about the critical role of bacteria in the oral cavity in response to nitrate supplementation and associated with a decrease in blood pressure [28]. Supplementation of beetroot juice had reduced systolic pressure by 2.8 mmHg in younger subjects whereas 1.0 mmHg in the older age group [5].

The body mass index affects the success of supplementation of beetroot juice against blood pressure. Several studies on this systematic review examined obese subjects. Siervo [5], Jajja[25], and Ashor [29] whose research subjects were overweight or even obese showed positive results. Another study by Raubenheimer [20] also stated that beetroot juice supplementation could reduce systolic blood pressure in older adults who are overweight. A meta-analysis conducted by Bahadoran [33] stated that subjects who had a body mass index > 25 had a more significant decrease in systolic blood pressure compared to subjects with a normal body mass index (211.3 compared with 26.0 mm Hg).

In this review, there were five studies showing a greater effect in healthy subjects and one studies that find positive effects in patients with hypertension. Bondonno [24] had not found significant effect in reducing blood pressure in hypertensive patients who were taking antihypertensive medication after one week beetroot juice supplementation. The use of antihypertensive medication can affect the production of nitric oxide. Ormesher [28] also had not found a significant reduction on blood pressure in pregnant women with chronic hypertension after eighth day of intervention with beetroot juice. However, Asgary [19] found that the supplementation of raw beetroot juice decreased systolic blood pressure of 6.67 mmHg and a diastolic of 4.59 mmHg although statistically it did not show significant results when compared to cooked beet. Meanwhile, in healthy subjects, supplementation of beetroot juice showed significant result in decreasing blood pressure [20, 25, 26, 27, 29]. These results indicated that beetroot juice supplementation in healthy subjects may be associated to greater reductions in blood pressure than in hypertensive subjects. These findings are inconsistent with research showing that antihypertensive effect of pomegranate juice more likely to be elicited in hypertensive patients [34].

The duration of beetroot juice supplementation is given in a variety of time frames, ranging from the acute (short time) to chronic (long time). Acute supplementation is given in 3-24 hours, while chronic supplementation is given at least 1 week and at most 4 weeks. The duration of supplementation did not affect the success of supplementation of beetroot juice. Research divided the subjects into 3 groups with the time of giving beetroot juice for 3 weeks, 2 weeks, and 1 week, but there were no significant differences in results from the three groups [5]. In contrast, a study that provided beetroot juice supplementation for 24 hours showed a decrease in systolic blood pressure of 5 mmHg and diastolic 3-4 mmHg [27]. The best duration of beetroot juice supplementation is over two weeks [17].

The nitrate concentration in beetroot juice supplementation varied in each study. Overall, the nitrate levels were given in the range of 14-12.9 mmol or equivalent to 300-500 mg. Normally, the average intake of nitrates from food sources (especially vegetables) was 1.5 to 2 mmol daily, and WHO (*World Health Organization*) sets a daily intake of nitrate that can be consumed per day is 3.7 mg/kg or equivalent to 4.2 mmol daily for 70 kg individuals due to concerns about methemoglobinemia and carcinogenesis [26]. The correlation of concentrations of nitrate to a decrease in blood pressure needs

to be further investigated because in several studies showed insignificant results on changes in blood pressure despite large nitrate intake in comparison with placebo (nitrate-depleted beetroot juice) [5, 21, 28].

In general, the volume of beetroot juice does not make a significant difference in reducing blood pressure. A study by Raubenheimer [20] who provided 140 mL of beetroot juice with 12.9 mmol/L nitrate content showed the most significant reduction in blood pressure among the nine other studies in this review. The result showed a decrease in systolic blood pressure by 7.9 mmHg and a diastolic 5.7 mmHg. Meanwhile, 250 mL of beetroot juice showed a decrease in systolic blood pressure by 7.7 mmHg after 24 hours and four weeks, also 5.2 mmHg and 2.4 mmHg diastolic blood pressure after 24 hours and four weeks respectively [26]. Single 500 g of beetroot and apple juice, a greater reduction in SBP (4–5 mm Hg) is achieved after drinking BJ compared with apple juice at 6 h in healthy volunteers. [35]. This showed that supplementation of beetroot juice with more volume does not guarantee success in lowering the blood pressure.

Dietary beetroot juice supplementation and its relevance in reduction of blood pressure must be analyzed. Several studies have shown that consumption of nitrate (NO_3^-) has potency to reduce the risk of high blood pressure, stroke and coronary heart disease. A decrease of 2-5 mmHg in systolic blood pressure can reduce the risk of death by 7% and the risk of stroke by 10-14% and coronary heart disease by 7-9% [19]. It should be emphasized that the administration of beetroot juice on the subject in this systematic review did not show any side effects and was safely given to the subjects, even to pregnant women [20]. This review concludes that the administration of high nitrate content through beetroot juice supplementation has the potential as alternative hypertension.

Beetroot juice is less effective if given to old people, and many factors may influence it. The changes in oral microflora can affect the efficiency of bacterial reductase activity in the change of NO_3^- to NO_2^- , stomach acid production also decreases as age increases which affect the formation of Nitric Oxide and reduce sensitivity of vascular smooth muscle cells to the effects of nitric oxide dilatation [5, 29]. Interfering factors that can be controlled in the research of beetroot juice supplementation such as physical activity, use of antihypertensive drugs, smoking habits, use of oral cleansing fluid, consumption of caffeine, and chewing gum [5, 21, 27].

The limitation of the research regarding beetroot juice supplementation in decreasing blood pressure is that there are many different results regarding its effectiveness. Most studies on beetroot juice on blood pressure have only discussed potency of the nitrate reduction process to nitric oxide even though many other ingredients can be potential antihypertensive agents such as betalain and flavonoids. Moreover, the previous studies were still limited to test effect of long-term beetroot juice supplementation on blood pressure reduction. Therefore, further clinical studies with different bioactive components in beetroot juice are needed to confirm potency of beetroot juice for treating hypertension.

CONCLUSION

Beetroot juice supplementation is not so useful on reducing blood pressure because it only has an acute effect in lowering blood pressure. The concentration of nitrate which has undergone a reduction into nitrite in beetroot can give effect to lower blood pressure, especially on systolic blood pressure. It seems promising but it appears the efficacy of beetroot juice supplementation influenced by several factors, including gender, age, nutritional status (BMI), initial blood pressure, and duration of supplementation, dose, and concentration of nitrate. Hence, further studies are recommended to study the blood pressure lowering effect of other bioactive components in beetroot juice.

CONFLICT OF INTEREST

Authors state that there is no conflict of interest with either the company, the publisher or the previous author of articles in this review.

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